SUMMARY OF PRODUCT CHARACTERISTICS

for

Galli Ad, 0.74 -1.85 GBq, radionuclide generator

1. NAME OF THE MEDICINAL PRODUCT

Galli Ad, 0.74 -1.85 GBq, radionuclide generator

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The radionuclide generator contains germanium (^{68}Ge) as mother nuclide which decays to the daughter nuclide gallium (^{68}Ga).
The germanium (^{68}Ge) used for the production of the (^{68}Ge/^{68}Ga) generator is carrierfree.
The total radioactivity due to germanium (^{68}Ge) and gamma-ray-emitting impurities is not more than 0.001%.
The Galli Ad 0.74 – 1.85 GBq radionuclide generator is a system for the elution of gallium (^{68}Ga) chloride solution for radiolabelling in accordance with Ph. Eur 2464. This solution is eluted from a column on which the mother nuclide germanium (^{68}Ge) , parent of gallium (^{68}Ga) is fixed. The system is shielded. Physical characteristics of both mother and daughter nuclides are summarized in Table 1.

Table 1: physical characteristics of ^{68}Ge and ^{68}Ga

	Physical characteristics of	
	^{68}Ge	**^{68}Ga**
Half-live	270.95 days	67.71 minutes
Type of decay	Electron capture	Positron emission
X-rays	9.225 (13.1 %) 9.252 (25.7 %) 10.26 (1.64 %) 10.264 (3.2 %) 10.366 (0.03 %)	8.616 (1.37 %) 8.639 (2.69 %) 9.57 (0.55 %)
Gammas		511 keV (178.28 %), 578.55 keV (0.03 %) 805.83 keV (0.09 %), 1077.34 keV (3.22 %) 1260.97 keV (0.09 %) 1883.16 keV (0.14 %)
beta+		Energy max. Energy 352.60 keV 821.71 keV (1.20 %) 836.00 keV 1899.01 keV (87.94 %)
Data derived from nudat (www.nndc.bnl.gov)		

1.1 ml of the Galli Ad eluate contains a potential maximum of 1850 MBq ^{68}Ga and 18.5 kBq ^{68}Ge (0.001 % breakthrough). This corresponds to 1.2 ng ^{68}Ga-gallium and 0.07 ng ^{68}Ge-germanium.

The quantity of gallium (^{68}Ga) chloride solution for radiolabelling Ph. Eur. that may be eluted from the generator is dependent on the quantity of germanium (^{68}Ge) chloride present and the lapsed time since the previous elution. If mother and daughter nuclides are in equilibrium more than 60 % of the present gallium (^{68}Ga) chloride can be eluted. A fixed volume of 1.1 mL (^{68}Ga) chloride solution is eluted.

Table 2 summarizes the activity on the generator and obtained by elution at the start of the shelf-life and at the end of the shelf-life.

Table 2: activity on the generator and obtained by elution

Strength	Activity inside generator at the start of shelf-life	Activity inside generator at the end of shelf-life	Eluted activity at the start of shelf-life*	Eluted activity at the end of shelf-life*
0.74 GBq	0.74 GBq ± 10 %	0.3 GBq ± 10 %	NLT 0.41 GBq	NLT 0.16 GBq
1.11 GBq	1.11 GBq ± 10 %	0.4 GBq ± 10 %	NLT 0.61 GBq	NLT 0.22 GBq
1.48 GBq	1.48 GBq ± 10 %	0.6 GBq ± 10 %	NLT 0.81 GBq	NLT 0.32 GBq
1.85 GBq	1.85 GBq ± 10 %	0.7 GBq ± 10 %	NLT 1.02 GBq	NLT 0.40 GBq

NLT = not less than
** in equilibrium*

More detailed explanations and examples for elutable activities at various time points are given in section 12.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Radionuclide generator

The generator is presented as a plastic case with an outlet port and a knob. The solution for elution is integrated inside the plastic case. The eluate can be collected at the outlet port or inserted directly into a synthesis apparatus.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is not intended for direct use in patients.

The eluate from the radionuclide generator (gallium (^{68}Ga) chloride solution) is indicated for *in vitro* radiolabelling of various kits for radiopharmaceutical preparation developed and approved for radiolabelling with such solution to be used for positron emission tomography (PET) imaging.

4.2 Posology and method of administration

This medicinal product is for use in designated nuclear medicine facilities only, and should only be handled by specialists experienced with *in vitro* radiolabelling.

Posology
The quantity of the eluate (gallium (^{68}Ga) chloride solution) required for radiolabelling and the quantity of ^{68}Ga-labelled medicinal product that is subsequently administered will depend on the medicinal product that is radiolabelled and its intended use. Refer to the Summary of Product Characteristics/package leaflet of the particular medicinal product to be radiolabelled.
One elution corresponds to a fixed volume of 1.1 mL.

Paediatric population
Please refer to the Summary of Product Characteristics/package leaflet of the ^{68}Ga-labelled medicinal product for more information concerning its paediatric use.

Method of administration
The gallium (^{68}Ga) chloride solution is not intended for direct use in patients but is used for *in vitro* radiolabelling of various kits for radiopharmaceutical preparation. The route of administration of the final medicinal product should be adhered to.

For instructions on extemporary preparation of the medicinal product before administration, see section 12.

4.3 Contraindications

Do not administer gallium (^{68}Ga) chloride solution directly to the patient.

The use of ^{68}Ga-labelled medicinal products is contraindicated in case of hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

For information on contraindications to particular ^{68}Ga-labelled medicinal products prepared by radiolabelling with gallium (^{68}Ga) chloride solution, refer to the Summary of Product Characteristics/package leaflet of the particular medicinal product to be radiolabelled.

4.4 Special warnings and precautions for use

Gallium (^{68}Ga) chloride solution is not to be administered directly to the patient but is used for *in vitro* radiolabelling of various kits for radiopharmaceutical preparation.

Individual benefit/risk justification
For each patient, the radiation exposure must be justifiable by the likely benefit.
The activity administered should in every case be as low as reasonably achievable to obtain the required effect.

General warnings
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicinal products refer to the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies of gallium (^{68}Ga) chloride solution with other medicinal products have been performed, because it is for radiolabelling of medicinal products.

For information concerning interactions associated with the use of ^{68}Ga-labelled medicinal products refer to the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radioactive medicinal products to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy

Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and foetus.

Breast-feeding

Before administering a radioactive medicinal product to a mother who is breast-feeding, consideration should be given to whether the investigation could be reasonably delayed until the mother has ceased breast-feeding. If the administration is considered necessary, breast-feeding should be interrupted for 12 hours and the expressed feeds discarded.

Further information concerning the use of a ^{68}Ga-labelled medicinal product in pregnancy and breast-feeding is specified in the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

Fertility

Further information concerning the use of a ^{68}Ga-labelled medicinal product concerning fertility is specified in the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

4.7 Effects on ability to drive and use machines

Effects on ability to drive and use machines following administration of ^{68}Ga-labelled medicinal products will be specified in the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.

4.8 Undesirable effects

Possible adverse reactions following the use of a ^{68}Ga-labelled medicinal product, will be dependent on the specific medicinal product being used. Such information will be supplied in the Summary of product Characteristics/package leaflet of the medicinal product to be radiolabelled.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Accidental administration of the eluate consisting of 0.1 mol/l hydrochloric acid may cause local venous irritation and, in case of paravenous injection, tissue necrosis. The catheter or affected area should be irrigated with isotonic saline solution.

No toxic effects are to be expected from the free ^{68}Ga after an inadvertent administration of the eluate. The administered free ^{68}Ga decays almost completely to inactive ^{68}Zn within a short time (97 % are decayed in 6 hours). During this time, ^{68}Ga is mainly concentrated in the blood/plasma (bound to transferrin) and in the urine. The patient should be hydrated to increase the excretion of the ^{68}Ga and forced diuresis as well as frequent bladder voiding is recommended.
Human radiation dose may be estimated using the information given in section 11.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other diagnostic radiopharmaceuticals, ATC code: V09X

The pharmacodynamic properties of ^{68}Ga-labelled medicinal products prepared by radiolabelling with Galli Ad prior to administration will be dependent on the nature of the medicinal product to be labelled. Refer to the Summary of Product Characteristics/package leaflet of the product to be radiolabelled.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Galli Ad in all subsets of the paediatric population on grounds of lack of significant therapeutic benefit over existing treatments (see section 4.2 for information on paediatric use). This waiver does however not extend to any diagnostic or therapeutic uses of the product when linked to a carrier molecule.

5.2 Pharmacokinetic properties

Gallium (^{68}Ga) chloride solution is not intended for direct use in patients but is used for *in vitro* radiolabelling of various kits for radiopharmaceutical preparation. Therefore, the pharmacokinetic properties of ^{68}Ga-labelled medicinal products will depend on the nature of the medicinal product to be radiolabelled.
Although gallium (^{68}Ga) chloride solution is not intended for direct use in patients, its pharmacokinetic properties were investigated in rats.

5.3 Preclinical safety data

The toxicological properties of ^{68}Ga labelled medicinal products prepared by radiolabelling with gallium (^{68}Ga) chloride solution, prior to administration, will depend on the nature of the medicinal product to be radiolabelled.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Matrix: Titanium dioxide.
- Integrated eluent: Sterile 0.1 mol/l hydrochloric acid.

6.2 Incompatibilities

Radiolabelling of carrier molecules with gallium (^{68}Ga) chloride is very sensitive to the presence of trace metal impurities.

It is important that all glassware, syringe needles etc., used for the preparation of the radiolabelled medicinal product are thoroughly cleaned to ensure freedom from such trace metal impurities. Only syringe needles with proven resistance to dilute acid should be used to minimise trace metal impurity levels.

It is recommended not to use uncoated chlorobutyl stoppers for the elution evacuated vial as they may contain considerable amounts of zinc that is extracted by the acidic eluate. As a general rule, when available, it is recommended to use the vials provided with the non-radioactive tracer to be labelled or a material identical or equivalent to that provided as a starter kit with the generator (see section 6.5 “accessories supplied with the generator”).

6.3 Shelf life

Radionuclide generator: 12 months from calibration date.
The calibration date and the expiry date are stated on the label.
Gallium (^{68}Ga) chloride eluate: After elution, immediately use the eluate.

6.4 Special precautions for storage

Radionuclide generator: Do not store above 25 °C.

Storage of radiopharmaceuticals should be in accordance with national regulations on radioactive materials.

6.5 Nature and contents of container

The column consists of a PEEK (polyetheretherketone) column which is attached to PEEK inlet and outlet lines via HPLC-style fittings. The inlet line is connected to the eluent container (PE/EVOH) via a dosing system (PE/EVA/PVC/PC/PTFE) and a C-flex line while the outlet line is connected to a union that pass through the outer case of the Galli Ad generator.

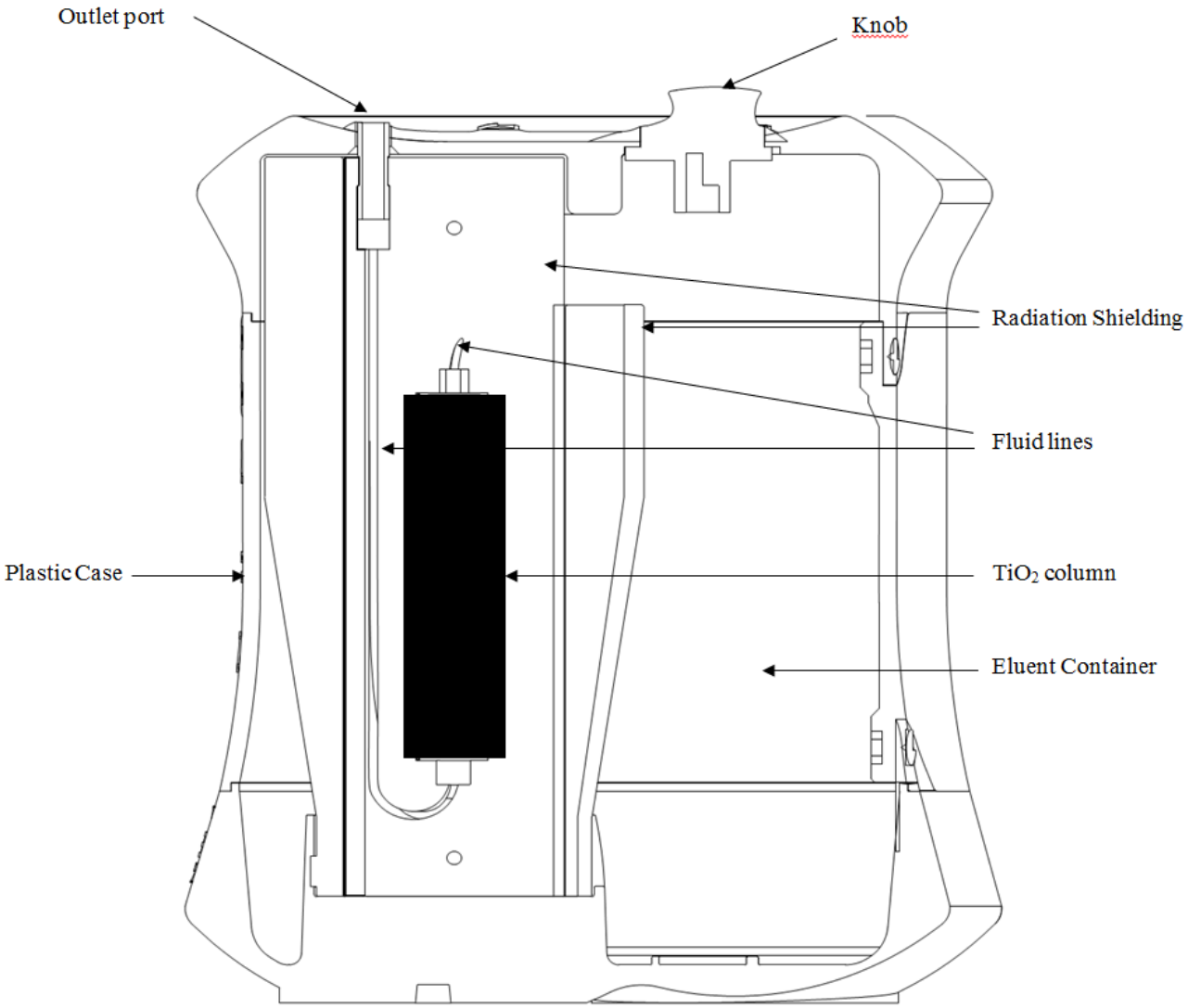
The column is contained within radiation shield assembly (Pb, W). The shield assembly and the eluent container are secured in a plastic outer box.

<u>Accessories supplied with the generator</u>

5 X 10 ml sterile evacuated vials ref: SVV-10A(Huayi)
5 X sterile tubing ref : 1155.03 or 1155.05 (Vygon)
5 X sterile needle 0.8 X 16mm 21G 5/8’’ ref : AN*2116R1 (Terumo)
5 X male male luer-lock connector ref : 893.00 (Vygon)

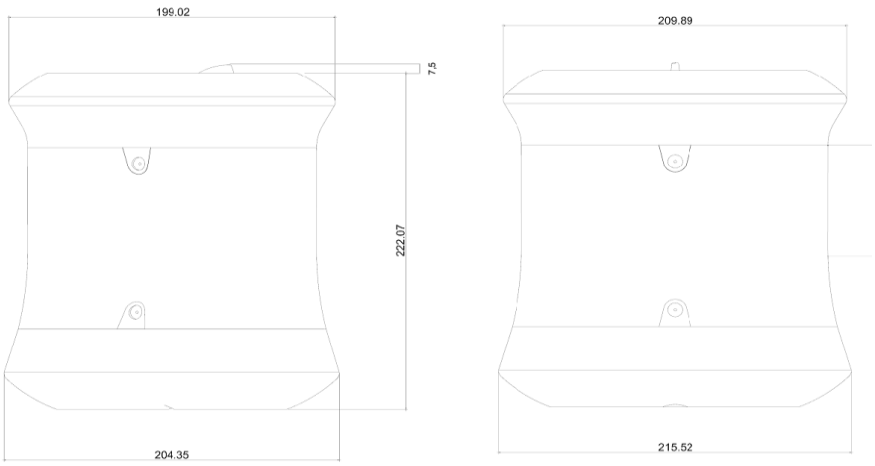
Pack sizes:
The radionuclide generators are supplied with the following ^{68}Ge activity amounts at calibration date: 0.74 GBq, 1.11 GBq, 1.48 GBq, 1.85 GBq. The integrated eluent volume (610 mL) allows for 450 elutions.

Sectional view of the Galli Ad radionuclide generator



3D view of the Galli Ad radionuclide generator

Size



Weight: approximately 16.5 kg

6.6 Special precautions for disposal and other handling

General warnings
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

The generator must not be disassembled for any reason as this may damage the internal components and possibly lead to a leak of radioactive material. Also, disassembly of the casing will expose the lead shielding to the operator.

Administration procedures should be carried out in a way to minimize risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Expired generators must be returned to IRE-ELiT. The residual activity of the generator must be estimated before return.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

IRE-ELiT
Avenue de l'Espérance
B-6220 Fleurus
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

To be implemented nationally

9. DATE OF FIRST AUTHORISATION

10. DATE OF REVISION OF THE TEXT

-

11. DOSIMETRY

The radiation dose received by the various organs following intravenous administration of a ^{68}Ga-labelled medicinal product is dependent on the specific medicinal product being radiolabelled. Information on radiation dosimetry of each different medicinal product following administration of the radiolabelled preparation will be available in the Summary of Product Characteristics of the particular medicinal product.

The dosimetry tables 3 and 4 below are presented in order to evaluate the contribution of non-conjugated ^{68}Ga to the radiation dose following the administration of ^{68}Ga-labelled medicinal product or resulting from an accidental intravenous injection of gallium (^{68}Ga) chloride solution.

The dosimetry estimates were based on a rat distribution study and the calculations were effected using OLINDA - Organ Level INternal Dose Assessment Code. Time points for measurements were 5 minutes, 30 minutes, 60 minutes, 120 minute, 180 minutes, and 360 minutes.

Table 3: Absorbed dose per unit activity administered –inadvertent administration in women

Absorbed dose per unit radioactivity administered (mGy/MBq)

Organ	Adult (57 kg)	15 years (50 kg)	10 years (30 kg)	5 years (17 kg)	1 year (10 kg)	Newborn (5 kg)
Adrenals	0.0114	0.0112	0.0164	0.0238	0.0403	0.0782
Brain	0.0180	0.0159	0.0176	0.0206	0.0292	0.0667
Breasts	0.0059	0.0058	0.0110	0.0163	0.0269	0.0545
Gallbladder Wall	0.0096	0.0092	0.0127	0.0201	0.0390	0.0750
LLI Wall	0.0032	0.0032	0.0050	0.0077	0.0133	0.0292
Small Intestine	0.0039	0.0039	0.0062	0.0099	0.0178	0.0376
Stomach Wall	0.0057	0.0056	0.0088	0.0133	0.0250	0.0502
ULI Wall	0.0040	0.0039	0.0067	0.0104	0.0199	0.0425
Heart Wall	0.1740	0.1940	0.3010	0.4830	0.8730	1.7200
Kidneys	0.0385	0.0421	0.0600	0.0888	0.1600	0.4150
Liver	0.0972	0.0974	0.1480	0.2200	0.4270	0.9890
Lungs	0.1860	0.2240	0.3190	0.4930	0.9840	2.7100
Muscle	0.0073	0.0076	0.0131	0.0319	0.0622	0.0954
Ovaries	0.0188	0.0203	0.0566	0.0988	0.2250	0.4590
Pancreas	0.0187	0.0218	0.0406	0.0547	0.1120	0.3400
Red Marrow	0.0225	0.0256	0.0415	0.0777	0.1770	0.5710
Osteogenic Cells	0.1160	0.1140	0.1840	0.3100	0.7350	2.3500
Skin	0.0029	0.0029	0.0044	0.0067	0.0122	0.0271
Spleen	0.0055	0.0056	0.0086	0.0130	0.0238	0.0492
Thymus	0.0100	0.0102	0.0133	0.0190	0.0297	0.0570
Thyroid	0.2210	0.2980	0.4600	1.0200	1.9300	2.6300
Urinary Bladder Wall	0.0023	0.0022	0.0038	0.0063	0.0110	0.0222
Uterus	0.0792	0.0802	1.3400	2.0300	3.6900	1.4700
Total Body	0.0177	0.0178	0.0289	0.0468	0.0920	0.2340
Effective Dose (mSv/MBq)	0.0483	0.0574	0.1230	0.2090	0.4100	0.7170

Table 4: Absorbed dose per unit activity administered – inadvertent administration in men

Absorbed dose per unit radioactivity administered (mGy/MBq)						
Organ	**Adult (70 kg)**	**15 years (50 kg)**	**10 years (30 kg)**	**5 years (17 kg)**	**1 year (10 kg)**	**Newborn (5 kg)**
Adrenals	0.0093	0.0112	0.0165	0.0235	0.0377	0.0749
Brain	0.0134	0.0137	0.0148	0.0170	0.0241	0.0563
Breasts	0.0062	0.0074	0.0142	0.0213	0.0350	0.0725
Gallbladder Wall	0.0081	0.0096	0.0137	0.0213	0.0409	0.0803
LLI Wall	0.0015	0.0020	0.0031	0.0051	0.0091	0.0204

Small Intestine	0.0022	0.0029	0.0048	0.0080	0.0146	0.0309
Stomach Wall	0.0048	0.0066	0.0099	0.0153	0.0287	0.0560
ULI Wall	0.0027	0.0033	0.0058	0.0094	0.0182	0.0385
Heart Wall	0.3030	0.3930	0.6110	0.9830	1.7800	3.4900
Kidneys	0.0198	0.0241	0.0345	0.0510	0.0911	0.2310
Liver	0.0766	0.1030	0.1570	0.2330	0.4500	1.0400
Lungs	0.1340	0.2000	0.2850	0.4390	0.8720	2.3800
Muscle	0.0051	0.0074	0.0129	0.0326	0.0636	0.0961
Pancreas	0.0187	0.0257	0.0480	0.0646	0.1310	0.4030
Red Marrow	0.0138	0.0154	0.0243	0.0441	0.0980	0.3110
Osteogenic Cells	0.0431	0.0558	0.0901	0.1510	0.3560	1.1300
Skin	0.0020	0.0024	0.0036	0.0057	0.0103	0.0232
Spleen	0.0041	0.0056	0.0084	0.0130	0.0227	0.0469
Testes	0.0011	0.0018	0.0075	0.0094	0.0138	0.0239
Thymus	0.0139	0.0158	0.0194	0.0276	0.0417	0.0794
Thyroid	0.1980	0.3250	0.5020	1.1200	2.1100	2.8800
Urinary Bladder Wall	0.0011	0.0013	0.0022	0.0039	0.0070	0.0152
Total Body	0.0115	0.0147	0.0237	0.0383	0.0748	0.1900
Effective Dose (mSv/MBq)	0.0338	0.0506	0.0756	0.1340	0.2600	0.5550

The effective dose resulting from an accidental intravenously injected activity of 250 MBq is 12.1 mSv for a 57-kg female adult and 8.45 mSv for a 70-kg male adult.

Data on the radiation dose to patients of gallium (^{68}Ga) citrate listed in the table 5 below are from ICRP 53 and may be used to estimate distribution after inadvertent application of unbound gallium (^{68}Ga) from the generator eluate, even though the data were obtained using a different salt.

Table 5: Absorbed dose per unit activity inadvertent administration of gallium (^{68}Ga)-Citrate

Absorbed dose per unit radioactivity administered of ^{68}Ga-Citrate (mGv/MBq)					
Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.034	0.044	0.064	0.088	0.140
Bone surface	0.037	0.048	0.080	0.140	0.310
Breast	0.014	0.014	0.023	0.037	0.074
LLI Wall	0.018	0.022	0.036	0.059	0.110
Small Intestine	0.064	0.080	0.140	0.230	0.450
Stomach Wall	0.014	0.017	0.027	0.044	0.084
ULI Wall	0.053	0.064	0.110	0.180	0.360
Kidneys	0.026	0.032	0.046	0.068	0.120
Liver	0.027	0.035	0.053	0.079	0.150
Lungs	0.013	0.016	0.025	0.041	0.080
Pancreas	0.014	0.018	0.029	0.047	0.089
Red Marrow	0.046	0.064	0.110	0.210	0.450
Spleen	0.036	0.051	0.080	0.130	0.240
Testes	0.013	0.015	0.024	0.039	0.077
Thyroid	0.012	0.015	0.025	0.042	0.081
Urinary Bladder Wall	0.014	0.016	0.026	0.044	0.081
Other tissue	0.013	0.015	0.025	0.041	0.080
Effective Dose (mSv/MBq)	0.027	0.034	0.056	0.095	0.190

External radiation exposure

The average surface or contact radiation for the (^{68}Ge/^{68}Ga) radionuclide generator is less than 0.054 µSv/h per MBq of ^{68}Ge. For example, a 1.85 GBq generator will reach a maximum average surface dose rate of 100 µSv/h. It is generally recommended that the generator is stored within auxiliary shielding to minimize dose to operating personnel.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Elution of the generator must be performed in premises complying with the national regulations concerning the safety of use of radioactive products.

Elution should be performed under aseptic conditions.

Unpacking of the generator

1. Check flight case for shipping damage. If damaged, perform radiation wipe survey of the damaged area. If the activity exceeds 40 becquerel per 100 cm^2, notify your Radiation Safety Officer.
2. Before opening the case, please refer to the arrow signs to make sure the shipping box is placed **in the right orientation**. Check that the security seals are not broken. Then cut the seals and open all toggle-type fasteners. Remove vertically the upper part of the flight case. Take out small removable foam dunnages from the lower part of the flight case in order to permit the extraction of the generator.
3. Carefully remove generator. Perform radiation survey.

CAUTION: Drop hazard: The Galli Ad generator weighs approximately 16.5 kg. Handle with care and firmly to avoid potential injuries. If generator is dropped or if shipping damage extends into the inner flight case, check for leaks and perform a wipe survey of the

generator.

4. Perform wipe survey of box inserts and generator outer surface. If wipes exceed 40 becquerel per 100 cm^2, notify your Radiation Safety Officer.
5. Check the whole casing and outlet port and seal for damage.
6. Do not remove the port plug before installing the generator nor before being ready for elution.

Optimal positioning:

1. Generator must always stand in a vertical position i.e. so that the green control button faces upwards.
2. When installing the Galli Ad radionuclide generator in its final position, i.e. with a synthesis device or for manual elutions, it is recommended to keep the outlet line as short as possible (maximum 50 cm) as the length of this tubing may influence the recovered yield in the receiving/reaction vial.
3. Local shielding is recommended (especially when performing an elution) and personal protective equipment, eye and hand protection, must be used.

Preparation :

1. **Aseptic working technique must be applied when using the generator, especially when handling the elution port. This is critical for the maintenance of sterility.**

The attachment of tubing, elution needles, in the elution of the generator and other activities potentially exposing the internal surfaces of generator to the environment should be undertaken using aseptic technique in an appropriately clean environment according to current national requirements. In particular, use of gloves and sterile cleaning of the vials is mandatory before use. In case the vial is to be opened and closed, the stopper should be put upside down on the bench.

2. Unscrew manually the cap from the luer lock connector (fig. 1).

Fig.1

3. Connect manually a **sterile tubing** (extension line) to the luer lock connector (fig. 2). *For example, product number 1155.03 or 1155.05 from Vygon are suitable. Other sterile polyethylene tubing intended for parenteral use is suitable provided void volume is not more than 1mL.*

Fig.2

4. A. In case of use with a synthesis device, connect the other end of the tubing to the synthesis device. Avoid hard bending or pinching of the line.
   B. In case of manual elution, connect a sterile needle to the other end of the tubing using a male/male luer lock adapter (fig. 3). Avoid hard bending or pinching of the line.
   *For example, product number AN*2116R1 0.8 X 16mm 21G $^{5}/_{8}$ from Terumo and product number 893.00 from Vygon are suitable. Other sterile polyethylene tubing intended for parenteral use is suitable provided that the void volume is not more than 1mL.*

Fig.3

5. The Galli Ad generator is now ready for use.

<u>Elution:</u>

1. Prepare additional necessary materials:
   – Personal protective equipment: elutions should be performed while wearing eye and hand protection and also appropriate laboratory cloth.
   – Shielded receiving evacuated sterile 10 ml vial in case of manual elution. Avoid uncoated chlorobutyl stoppers as they may contain considerable amounts of zinc that is extracted by the acidic eluate. As a general rule, when available, it is recommended to use the vials provided with the non-radioactive tracer to be labelled or a material identical or equivalent to that provided as a starter kit with the generator. These accessories are:

5 X 10 ml sterile evacuated vials ref: SVV-10A(Huayi)
5 X sterile tubing ref : 1155.03 or 1155.05 (Vygon)
5 X sterile needle 0.8 X 16mm 21G 5/8'' ref : AN*2116R1 (Terumo)
5 X male male luer-lock connector ref : 893.00 (Vygon)

– In case of use of an automatic radiosynthesis module, it is recommended to place a single-use sterile check-valve between the male/male luer lock adapter and the automatic radiosynthesis unit. *For example, product number MX745-01 from Smiths Medical is suitable.*

2. **Aseptic working technique must be maintained during the assembly process, especially when handling the ports. This is critical for the maintenance of sterility.**
3. Turn the green button by 90° to the loading position and wait for at least 10 seconds (fig.4).

Fig.4

4. Then, turn back the button by 90° to its initial position (fig. 5).

Fig.5

5. The generator is now ready for elution either manually or by a synthesis module. In the latter case please go directly to step 8 after the labelling has been performed by the synthesis module.
6. Remove the cap from the needle and quickly pierce vertically right in the center of the septum of a shielded sterile evacuated elution vial (fig.6). Wait for at least 3 minutes for the elution process to take place (a fixed volume of 1.1 mL is eluted) and for the line to be drained by air. Please use local shielding or radioprotection mean as the activity will be transferred from the generator to the vial. Measure solution with a calibrated dose calibrator to determine the yield. Please decay correct the measured activity to the starting time of elution.

   CAUTION :10 ml capacity sterile evacuated vials are suitable but it is recommended to avoid contact of the eluate with uncoated halobutyl stoppers as they may contain important amounts of zinc that might prevent a subsequent radiolabelling step.

Fig.6

7. Remove the needle from the vial and place the cap (fig. 7 and 8).

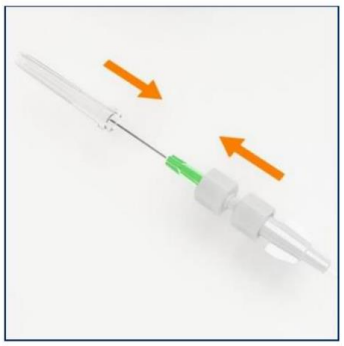


Fig.7 Fig.8

8. Disconnect manually the tubing from the luer lock connector and **place the cap in order to obturate the generator outlet** (fig. 9 and 10).

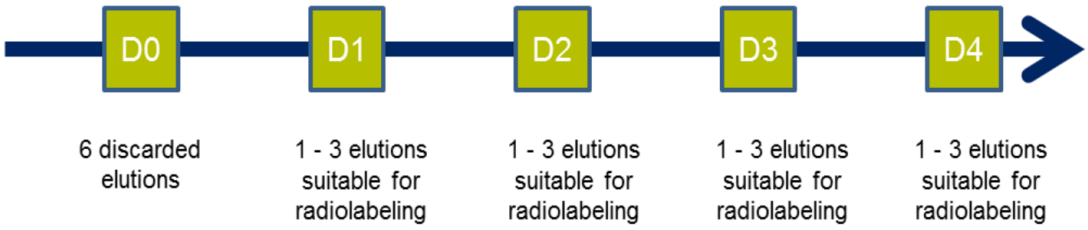
Fig.9 Fig.10

IMPORTANT: In case the button was not turned back to the elution position after having been put in the loading position for more than 6 hours, the eluate must be discarded.

First use of the generator :

IMPORTANT: When using the generator for the first time, **a conditioning procedure must be performed** once before using it for radiolabeling purposes. It consists of **six consecutive discarded elutions to be carried-out within 24 hours.** These elutions can be performed in a row (one directly after the other) if desired. After that, the next generator eluates are suitable for radiolabeling purposes provided that they come from an elution performed within 24 hours since the last elution. **This conditions only applies to the first eluates intended for radiolabeling during the**

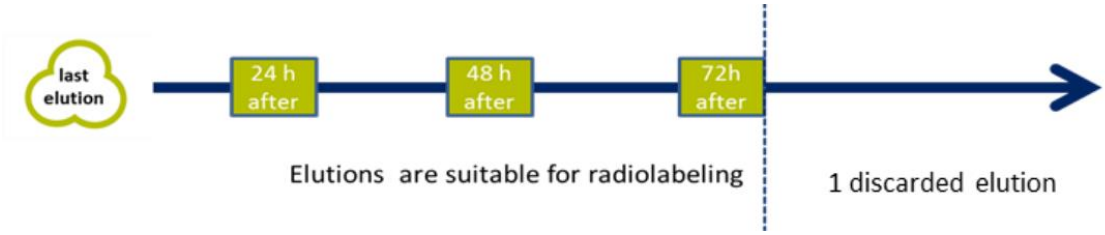
first four days (i.e. typically only during the first week of use of the generator).



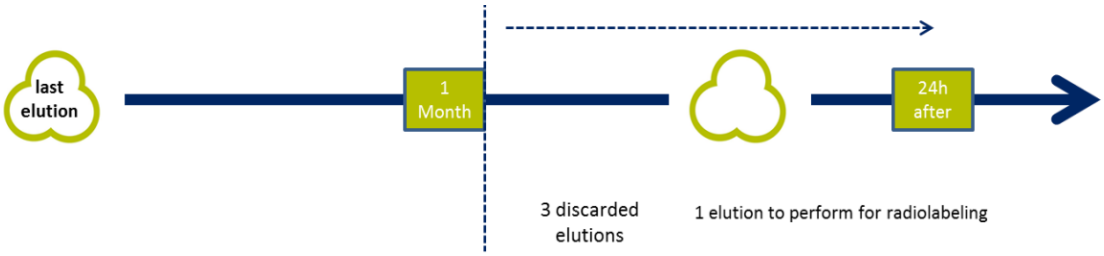
It is recommended to test the eluate for ^{68}Ge breakthrough after the first 6 conditioning discarded elutions by comparing the activity level of the ^{68}Ga and the ^{68}Ge. For further details on the method, please refer to Ph. Eur. Monograph #2464. Breakthrough should be tested at the moment the generator comes into operation (after the foreseen 6 conditioning elutions), and after six months of use.

Continuous routine elution:

During the shelf life of the generator, all eluates are suitable for direct radiolabeling provided that a previous elution has been performed **within the last 72 hours**. In case a radiolabeling is intended and the generator has not been eluted within that interval, it is recommended to perform one discardable elution beforehand.



If the generator is not eluted for **more than a month**, **three consecutive discarded elution are to be performed** and the first eluate intended for radiolabeling should be extracted within the next 24 hours.



The solution eluted is a clear, sterile and colourless gallium (^{68}Ga) chloride solution, with a pH between 0.5 and 2.0 and a radiochemical purity greater than 95 %. Check the clarity of the eluate before use and discard it if the solution is not clear.

IMPORTANT: In case the column has not been drained completely (due to e.g. unsatisfactory vacuum in the vial), a new vacuum vial can be connected to the generator outlet (via tubing, connector and needle) for one minute. In this case, the green button on the generator needs to be in the elution/standby position. This operation will finalize the draining. The content of the new vial can be used if it is used immediately. If not, it has to be discarded.

Galli Ad elution yield

The activity stated on the label of the Galli Ad generator is expressed in ^{68}Ge available at the calibration date (12:00 CET). The available ^{68}Ga activity depends on the ^{68}Ge activity at the time of elution and the elapsed time since the previous elution.

A Galli Ad generator in full equilibrium yields more than 55 % of ^{68}Ga.

The output will decrease with decay of the ^{68}Ge parent over time. For example, after 9 months' decay (39 weeks), the ^{68}Ge will be reduced by 50 % (see Table 6).

Table 6: Decay Chart for ^{68}Ge

Elapsed Time in weeks	Decay Factor	Elapsed Time in weeks	Decay Factor
1	0.98	27	0.62
2	0.96	28	0.61
3	0.95	29	0.59
4	0.93	30	0.58
5	0.91	31	0.57
6	0.90	32	0.56
7	0.88	33	0.55
8	0.87	34	0.54
9	0.85	35	0.53
10	0.84	36	0.52
11	0.82	37	0.52
12	0.81	38	0.51
13	0.79	39	0.50
14	0.78	40	0.49
15	0.76	41	0.48
16	0.75	42	0.47
17	0.74	43	0.46
18	0.72	44	0.45
19	0.71	45	0.45
20	0.70	46	0.44
21	0.69	47	0.43
22	0.67	48	0.42
23	0.66	49	0.42
24	0.65	50	0.41
25	0.64	51	0.40
26	0.63	52	0.39

After an elution of the Galli Ad generator the ^{68}Ga will be build up by the continuous decay of the parent ^{68}Ge. The generator requires at least 7 hours to achieve almost full yield after being eluted, but in practice it is also possible to elute the generator after 3 hours.

Table 7 shows the build-up factor of activity of ^{68}Ga which can be eluted after times varying from 0 to 410 minutes since the previous elution:

Table 7: Build-up factors of ^{68}Ga

Elapsed Time in minutes	Build-Up Factor	Elapsed Time in minutes	Build-Up Factor
0	0.00	210	0.88
10	0.10	220	0.89
20	0.19	230	0.91
30	0.26	240	0.91
40	0.34	250	0.92
50	0.40	260	0.93
60	0.46	270	0.94
70	0.51	280	0.94
80	0.56	290	0.95
90	0.60	300	0.95
100	0.64	310	0.96
110	0.68	320	0.96
120	0.71	330	0.97
130	0.74	340	0.97
140	0.76	350	0.97
150	0.78	360	0.97
160	0.81	370	0.98
170	0.82	380	0.98
180	0.84	390	0.98
190	0.86	400	0.98
200	0.87	410	0.98

Examples
A 1.85 GBq generator is 12 weeks old. According to table 6, the activity of ^{68}Ge on the column can be calculated as follows:

1.85 GBq x 0.81 = 1.499 GBq

In full equilibrium the activity of ^{68}Ga on the column is also 1.499 GBq.

The generator is eluted and the collected ^{68}Ga activity is 1.049 GBq which corresponds to a typical yield of 70 %.

The same generator is eluted 4 hours later. The 7 hours needed to reach the ^{68}Ge / ^{68}Ga-equilibrium have not elapsed and the ^{68}Ga activity build up on the column can be calculated according to table 7 as follows:

1.499 GBq x 0.91 = 1.364 GBq

With a typical yield of 70 % ^{68}Ga, the collected activity would be:

1.364 GBq x 0.70 = 955 MBq

Note:
The activity of ^{68}Ga in the eluate can be measured to check the quality with regard to identity and content. The activity should be measured immediately after elution, but may also be measured up to 5 half-life periods after elution.

Due to the short half-time of ^{68}Ga which is 67.71 minutes, the elapsed time between the elution and the measurement of the activity has to be decay corrected to determine the actual yield at the elution time with the decay chart of ^{68}Ga, table 8.

Example
A new 1.85 GBq generator is eluted. The activity of ^{68}Ga measured 10 minutes after the elution was 1.169 GBq.

The yield at the time of the elution can be obtained by dividing the measured activity by the corresponding factor of the elapsed time stated in table 8:
1.169 GBq / 0.903 = 1.295 GBq

This corresponds to a yield of ^{68}Ga of 70 % at the time of the elution:
1.295 GBq / 1.85 GBq x 100 % = 70 %

Table 8: Decay chart of ^{68}Ga

Elapsed Time in minutes	Decay Factor	Elapsed Time in minutes	Decay Factor
1	0.990	35	0.700
2	0.980	36	0.693
3	0.970	37	0.686
4	0.960	38	0.679
5	0.950	39	0.672
6	0.941	40	0.665
7	0.931	41	0.658
8	0.922	42	0.652
9	0.912	43	0.645
10	0.903	44	0.639
11	0.894	45	0.632
12	0.885	46	0.626
13	0.876	47	0.619
14	0.867	48	0.613
15	0.868	49	0.607
16	0.850	50	0.601
17	0.841	51	0.595
18	0.832	52	0.589
19	0.824	53	0.583
20	0.816	54	0.577
21	0.807	55	0.571
22	0.799	56	0.565
23	0.791	57	0.559
24	0.783	58	0.554
25	0.775	59	0.548
26	0.767	60	0.543
27	0.759	61	0.537
28	0.752	62	0.532
29	0.744	63	0.526
30	0.737	64	0.521
31	0.729	65	0.516
32	0.722	66	0.510
33	0.714	67	0.505
34	0.707	68	0.500

Quality control
Clarity as well as pH (≤2) of the solution and the radioactivity must be checked before radiolabelling.

^{68}Ge breakthrough
A small amount of ^{68}Ge is washed from the column with each elution. ^{68}Ge breakthrough is expressed as a percentage of total ^{68}Ga eluted from the column, corrected for decay. The ^{68}Ge breakthrough is not more than 0.001 % of the eluted ^{68}Ga activity. When used according to instructions here above, the breakthrough stays below 0.001 % for the entire shelf life of the generator (12 months). For testing the ^{68}Ge breakthrough the activity level of the ^{68}Ga and the ^{68}Ge in the eluate should be compared. For further details please refer to the current version of the Ph. Eur. monograph 2464.

Warning: Breakthrough of ^{68}Ge can increase above 0.001 % if the generator is not eluted for more than 72 hours. If the generator has not been used for 72 or more, it should be pre-eluted (1 discarded elution). If the generator has not been eluted for more than a month 3 discarded elutions are to be performed and the first eluate intended for radiolabeling should be extracted within the next 24 hours.